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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/738,378	12/17/2003	Francisco Javier Canada Vicinay	2798-1-001	7275
7590 KLAUBER & JACKSON 4th Fl. 411 Hackensack Avenue Hackensack, NJ 07601			EXAMINER UNDERDAHL, THANE E	
			ART UNIT 1651	PAPER NUMBER
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		04/09/2007	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/738,378	VICINAY ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Thane Underdahl	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 13 December 2006.  
 2a) This action is FINAL.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-39 is/are pending in the application.  
 4a) Of the above claim(s) 33,35 and 38 is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 1-32,34 and 36-39 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date: _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date: _____   | 6) <input type="checkbox"/> Other: _____                          |

## DETAILED ACTION

This action is in response to the remarks filed on 12/13/06. Claims 1-39 are pending. Claims 33,35 and 38 are withdrawn as being drawn to non-elected species. Claims 1 and 20 have been amended. No new claims have been added.

### ***Response to Objections***

The objection to claim 1 is withdrawn in view of the applicant's amendment.

### ***Response to Claim Rejections - 35 USC § 112***

The rejection of claim 20 is withdrawn in view of applicant's amendment.

### ***Response to Claim Rejections - 35 USC § 103***

In response to the applicant's traversal of the 35 U.S.C § 103 rejection of claims 1, 2, 3, 4, 21-24, 27-32, 34, 36, 37, and 39 over Reyes et al (U.S. Patent # 5, 994, 092) in view of Ponpipom et al. (U.S. Patent # 4, 228,274), and Crumpton et al. (Biochem J. 70(4) 1958, page 729) as supported by Chemindustry.com, the Applicant's arguments were considered but not found persuasive.

The applicant argues that "the chemistry of carbohydrates is very complex" and that "Small changes in the structure of carbohydrates...can give rise to differences, both in their chemical reaction and in their behavior in the purification processes" (Applicant's Response page 10 and 11). The Applicant submits two additional articles by Marcaurelle et al. and Holemann et al. as supporting references. The examiner does not deny that the chemistry of carbohydrates is complex, however the rejection is based on the method of producing a 4GPX by a known enzymatic process and purifying the

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compound via crystallization. While the examiner respects the accomplishments of the applicant these arguments are not commensurate with the scope of the claims.

The applicant further argues that the customary sugars used in crystallization are "low molecular weight alcohols, water, ethyl acetate, hexane, and their mixtures...Crumpton et al. use acetone". However this not the entirety of what Crumpton et al. teaches. Crumpton et al. explicitly teach the use of aqueous acetone for recrystallization of low molecular weight sugars (Crumpton et al., page 732, col 2, paragraph 1).

Furthermore the applicant argue that they receive a desired purity of >99% of their 4GPX product. However this is not supported in the specification. The examiner did not find in the examples or specifically stated in the specification that this level of purity was obtained. Indeed the specification makes references to obtaining pure 4GPX (Applicant's Specification, page 17, paragraph 56, page 18 paragraph 58, page 20, paragraph 62, page 24, paragraph 71) but does not quantify the quality or magnitude of that purity as a ratio or percent. In addition in the Example 3 the Applicant only mentions using MeOH/acetone to recrystallization the product and gives no indication to what is the solvent ratio used for this recrystallization.

In summary the Applicant's arguments have been considered however a showing to overcome a prima facie case of obviousness must be clear and convincing (*In re Lohr et al.* 137 USPQ 548) as well as commensurate in scope with the claimed subject matter (*In re Lindner* 173 USPQ 356; *In re Hyson*, 172 USPQ 399 and *In re Boesch et al.*, 205 USPQ 215 (CCPA 1980). The Applicant does not provide evidence in the

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specification or the articles by Marcaurelle et al. and Holemann et al. to overcome a *prima facie* case of obviousness since all of the above do not establish unexpected results based on the solvent ratios limited in the claim for the recrystallization of 4GPX.

Therefore the following rejection is upheld and is repeated here. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 2, 3, 4, 21-24, 27-32, 34, 36, 37, 39 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Reyes et al (U.S. Patent # 5, 994, 092) in view of Ponpipom et al. (U.S. Patent # 4, 228,274), and Crumpton et al. (Biochem J. 70(4) 1958, page 729) as supported by Chemindustry.com ([www.chemindustry.com](http://www.chemindustry.com)).

These claims are drawn to a method of production of 4-O- $\beta$ -D-galactopyranosyl-D-xylose and purification from an enzymatic reaction between  $\sigma$ -nitrophenyl- $\beta$ -galactopyranoside and xylose with  $\beta$ -galactosidase acting as the catalyst.

The patent of Reyes et al. teach a method for the preparation of 4-O- $\beta$ -D-galactopyranosyl-D-xylose (4GPX) (See example 1, col 4). This method adds  $\sigma$ -nitrophenyl- $\beta$ -galactopyranoside to xylose in buffered water at pH=7 with  $\beta$ -galactosidase from *E. coli* into a reaction mixture. The reaction mix is incubated for 5 hours and 45 mins at 25 °C. After that time the reaction is heated to 100°C for 10 mins

and concentrated before being filtered on an activated carbon column with a water/ethanol gradient. This gradient isolates the 4-O-  $\beta$ -D-galactopyranosyl-D-xylose.

Claims 22-24 pertain to the amounts of D-xylose (claim 22),  $\beta$ -galactopyranoside (claim 23) and  $\beta$ -galactosidase (claim 24) added to the reaction solution. Reyes et al. already discusses the addition of these components in Example 1 in their patent (col 4 to col 5). Slight adjustments to the concentrations of the reaction mixture are rendered obvious in the absence of unexpected results or teachings of criticality since one of ordinary skill in the art would routinely optimize the reaction based on efficient use of enzyme and substrates to improve the cost to yield ratio.

Claims 27-31 pertain to the temperature conditions for the reaction of claim 1, which includes the following temperature ranges: constant temperature (claim 27), -5 °C to 40 °C (claim 28), lower than 0 °C (claim 29), -5 °C (claim 30), room temperature (claim 31). Reyes et al. teach in Example 1 of their patent (col 4 to col 5) that the reaction can be performed at constant room temperature (25 °C). One of ordinary skill in the art would recognize that the hydrolysis of the substrate,  $\sigma$ -nitrophenyl- $\beta$ -galactopyranoside by  $\beta$ -galactosidase will occur at any temperature in which the enzyme is active. This same artisan would also understand that the decrease of temperature will adjust the reaction rate. Therefore base on the time allotted for the reaction (i.e. performing the reaction overnight or over the lunch hour) one of ordinary skill in the art, through routine optimization would adjust the temperature accordingly.

Reyes et al. does not teach the crystallization of 4GPX. However crystallization is a common procedure for the purification of saccharides as taught by Ponpipom et al.

who crystallized glycopyranosides in either cold water or acetone (col 3, line 50).

Ponpipom et al. also teach that it is also possible to crystallize other glycopyranosides after a filtration step with diatomaceous silica (col 13, line 50) in solvents such as ethanol (col 10, line 68) or 2-propanone (col 13, line 44) or solvent mixtures such as ethyl acetate/ethyl ether (col 12, line 30). Diatomaceous silica is a synonym for Celite as supported by Chemindustry.com. Crumpton et al. teach that a disaccharide can be crystallized with aqueous acetone. With all these options available for the crystallization of saccharides, one of ordinary skill in the art would recognize that recrystallization is a common process for the isolation of saccharides and that the selection of solvent or mixture of solvents is a matter of routine optimization that depends on temperature, purity of the solvent and miscibility of the solvent systems used in the crystallization. Absent any teachings of criticality of the solvent selected and unexpected results one of ordinary skill in the art would have reasonable expectation of success in crystallizing disaccharides with the current available art. Please see M.P.E.P. § 2144.05 (II) for further support.

In response to the applicant's traversal of the 35 U.S.C § 103 rejection of claims 1, 5, 6, and 16-19 over Reyes et al (U.S. Patent # 5, 994, 092) in view of Ponpipom et al. (U.S. Patent # 4, 228,274), and Crumpton et al. (Biochem J. 70(4) 1958, page 729) as applied above and in further view of Wong-Madden et al. (U.S. Patent # 5,770,405) and Dahmen et al. (U.S. Patent # 4,675,392), the applicants arguments were considered but not found persuasive.

Applicant argues that the solvent system taught by Wong-Madden et al. is for chromatography on silica gel and not Active carbon. However as mentioned in the rejection, Reyes et al. does teach the use of a water/ethanol gradient to elute 4GPX from an activated carbon column and Wong-Madden et al. uses a similar solvent system of water/isopropanol/ethanol on silica gel. One of ordinary skill in the art would recognize from these references that the same solvent systems used for a silica gel column would work for an active carbon column since in the purification of disaccharides. Absent any evidence to the contrary the rejection is upheld

The applicant further argues that the use of isopropanol/water mixtures require less elution volume than methanol/water or ethanol/water. However there is not support for this statement in the specification. This argument is merely the argument of counsel and is unsupported by evidence or declarations of those skilled in the art. Attorney argument is not evidence unless it is an admission, in which case, an examiner may use the admission in making a rejection. See M.P.E.P. § 2129 and § 2144.03 for a discussion of admissions as prior art. Counsel's arguments cannot take the place of objective evidence. *In re Schulze*, 145 USPQ 716 (CCPA 1965); *In re Cole*, 140 USPQ 230 (CCPA 1964); and especially *In re Langer*, 183 USPQ 288 (CCPA 1974). See M.P.E.P. § 716.01(c) for examples of attorney statements that are not evidence and that must be supported by an appropriate affidavit or declaration.

In summary the rejection above is upheld in the absence of evidence to the contrary concerning the obviousness of the solvent system used by Wong-Madden et al. on an activated carbon column. Also the argument that the selection of

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isopropanol/water as a superior eluent to ethanol/water or methanol/water is not supported by the specification or other articles by those of ordinary skill in the art.

Therefore the following rejection is upheld and is repeated here. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 5, 6, and 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reyes et al (U.S. Patent # 5, 994, 092) in view of Ponpipom et al. (U.S. Patent # 4, 228,274), and Crumpton et al. ( Biochem J. 70(4) 1958, page 729) as applied above and in further view of Wong-Madden et al. (U.S. Patent # 5,770,405) and Dahmen et al. (U.S. Patent # 4,675,392).

These claims pertain to a method of isolation of 4GPX via a solid-liquid extraction using a column with an eluent and gradient of water/isopropanol.

Reyes et al., Ponpipom et al., and Crumpton et al. teach the enzyme assisted synthesis and purification via an activated carbon column and crystallization of 4GPX as detailed above.

Reyes et al. does teach the use of a water/ethanol gradient to elute 4GPX from an activated carbon column but not water/isopropanol as limited in claims 5 and 6. However Wong-Madden et al. (U.S. Patent # 5, 770,405) shows that solvent mixes of water/isopropanol/ethanol are suitable for the separation of oligosaccharides (col 12, table 2). It would be obvious to one skilled in the art to replace ethanol in the method of

Reyes et al. with isopropanol since Wong-Madden et al. shows that these act as art defined equivalents for the separation of saccharides.

Claims 16-19 discuss the purification of 4GPX on an activated carbon column which is taught by Reyes et al. (Example 1, col 5, line 3) who uses a solvent gradient of water/ethanol to elute 4GPX. As mentioned above Wong-Madden et al. shows that it is obvious to replace the water/ethanol gradient with an isopropanol/water solvent mixture. However neither directly teaches the specifics of the solvent gradient in claims 17 nor the amount of activated carbon to use in claim 18. These items are result effective variables optimized by routine experimentation by one or ordinary skilled in the art. The average skilled artisan would recognize that the solvent gradient will depend on the size of the column particles, the length and width of the column as well as the time allotted for the separation. The amount of activated carbon to use will depend on the perceived yield of 4GPX and the loading amounts of reaction mixture the column can bear to separate.

In response to the applicant's traversal of the 35 U.S.C § 103 rejection of amended claims 1, 7-15 over Reyes et al (U.S. Patent # 5, 994, 092) in view of Ponpipom et al. (U.S. Patent # 4, 228,274), Crumpton et al. ( Biochem J. 70(4) 1958, page 729) Wong-Madden et al. (U.S. Patent # 5,770,405) and Dahmen et al. (U.S. Patent # 4,675,392) as applied above and in further view of Rao et al. (Qual. Plant. - Pl.Fds.hum.Nutr. XXVIII 4:293-303, 1979) the Applicant's arguments were considered but not found persuasive.

The applicant argues that Rao et al. teach the extraction of fats from a specimen. However Rao also teach that once the fats are removed from the specimen using a non-polar chloroform solvent mix the samples still contain extractable free sugars that can be isolated by highly polar solvent system such as 70% ethanol. One of ordinary skill in the art would recognize that since there are many methods to perform an extraction and that the variables in solvent system and temperature will determine what and how a product such as a sugar is separated. It would be obvious to one of ordinary skill in the art that since Rao extracted fats from the sample using a soxhlet apparatus and that he can further extract free sugars with 70% ethanol that it would be obvious to use the same method to extract the free sugars using the new solvent 70% ethanol solvent system. The motivation comes from his previous success in extracting products from the same material.

Therefore the following rejection is upheld and is repeated here. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 7-15 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Reyes et al (U.S. Patent # 5, 994, 092) in view of Ponpipom et al. (U.S. Patent # 4, 228,274), Crumpton et al. (Biochem J. 70(4) 1958, page 729) Wong-Madden et al. (U.S.

Patent # 5,770,405) and Dahmen et al. (U.S. Patent # 4,675,392) as applied above and in further view of Rao et al. (Qual. Plant.-Pl.Fds.hum.Nutr. XXVIII 4:293-303, 1979).

These claims pertain to the method of extracting the 4GPX with celite and a Soxhlet extractor.

Claim 7 depends from claim 1 and limits the additional purification of the disaccharide to include the addition of celite and to the reaction mixture and extraction of the disaccharide with a Soxhlet extractor. Neither of these are taught by Reyes et al. However, the use of Soxhlet extractors and celite are known in the art as methods to purify saccharides as taught by Rao et al. (page 294, 3<sup>rd</sup> paragraph and 295 1<sup>st</sup> paragraph respectively) as well as previously mentioned by Ponpipom et al. above. Rao et al. also uses a non-polar/polar solvent mix of chloroform and methanol. However one of ordinary skill in the art would recognize that the main requirement for a solvent for Soxhlet extraction is that the compound be soluble in the hot solvent. It would be obvious to one skilled in the art to select other solvents or solvent mixes, known to dissolve saccharides such as those listed above by Ponpipom et al., or by those listed by Dahmen et al. who lists multiple solvents that other disaccharides are soluble in such as ethyl acetate (col 13, line 67) or solvent systems such as isoctane/ethyl acetate (col 14, line 42) for use in Soxhlet extraction. Again it would be a matter of routine optimization by the artisan to select solvents known in the art that dissolved saccharides (see M.P.E.P. § 2144.05 (II)) for Soxhlet extraction and absent any evidence to the criticality of solvent selection for the extraction or teaching of an unexpected result, one of ordinary skill in the art would have a reasonable expectation of success.

The amount of solvent used to elute the disaccharide from celite is also a matter of routine optimization by one of skill in the art. The volume of solvent to remove the disaccharide would depend on the size of the celite particles, the purity of the solvent and the temperature of the solvent and the amount of disaccharide absorbed on the celite.

Also a matter of routine optimization is the amount of celite to use in the extraction of the disaccharide. One of ordinary skill in the art would recognize that overloading the column would not accomplish the goal of purifying the disaccharide. Therefore this artisan would know the loading parameters of the celite or carbon-celite used in the experiment. He/she would also recognize that the loading amount of celite necessary for the purification would depend on the size and surface area of the celite particles. The skilled artisan would recognize that he/she must use the necessary amount of celite to purify the disaccharide base on the prospective yield. Larger reaction batches would require larger amounts of celite.

Claims 11 and 15 limit that the carbon in the activated carbon-celite column must be deactivated with HCl. One of ordinary skill in the art would recognize that the procedure for deactivating the column is a matter of routine optimization that would depend on the amount of the activated carbon in the column and the size of the column and recommendations from the manufacturer. It would also be dependent on the size and surface area of the carbon particles since this would determine how many theoretical plates were available for the adsorption and separation of the disaccharide.

In response to the applicant's traversal of the 35 U.S.C § 103 rejection of amended claims 25 and 26 over Reyes et al (U.S. Patent # 5, 994, 092) in view of Ponpipom et al. (U.S. Patent # 4, 228,274), Crumpton et al. ( Biochem J. 70(4) 1958, page 729), Dahmen et al. (U.S. Patent # 4,675,392), Rao et al. (Qual. Plant-Pl.Fds.hum. Nutr. XXVIII, 4: 1979, page 293) and Wong-Madden et al. (U.S. Patent # 5,770,405) in further view of Gabelsberger et al (FEMS Letters, 109(2-3), page 131, 1993), Fujimoto et al. (Glycogenjugate Journal 15, page 155, 1998) and Yoshitake et al.(Eur. J. Biochem. 101, page 395, 1979) the Applicant's arguments were considered but not found persuasive.

The Applicant argues that when the cosolvents are added to the reaction medium the yields are lower. This statement is not supported in the specification. This argument is merely the argument of counsel and is unsupported by evidence or declarations of those skilled in the art. Attorney argument is not evidence unless it is an admission, in which case, an examiner may use the admission in making a rejection. See M.P.E.P. § 2129 and § 2144.03 for a discussion of admissions as prior art. Counsel's arguments cannot take the place of objective evidence. *In re Schulze*, 145 USPQ 716 (CCPA 1965); *In re Cole*, 140 USPQ 230 (CCPA 1964); and especially *In re Langer*, 183 USPQ 288 (CCPA 1974). See M.P.E.P. § 716.01(c) for examples of attorney statements that are not evidence and that must be supported by an appropriate affidavit or declaration.

Therefore the following rejection is upheld and is repeated here. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 25 and 26 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Reyes et al (U.S. Patent # 5, 994, 092) in view of Ponpipom et al. (U.S. Patent # 4, 228,274), Crumpton et al. ( Biochem J. 70(4) 1958, page 729), Dahmen et al. (U.S. Patent # 4,675,392), Rao et al. (Qual. Plant-Pl.Fds.hum. Nutr. XXVIII, 4: 1979, page 293) and Wong-Madden et al. (U.S. Patent # 5,770,405) in further view of Gabelsberger et al (FEMS Letters, 109(2-3), page 131, 1993), Fujimoto et al. (Glycogenjugate Journal 15, page 155, 1998) and Yoshitake et al.(Eur. J. Biochem. 101, page 395, 1979).

These claims are drawn to the addition of cosolvents DMF, DMSO and dioxane to the reaction medium in the method of claim 1.

Reyes et al. and references listed above teach the method of claim 1 from which 25 and 26 depend. Reyes et al. teach the use of a phosphate buffer as the reaction solution but not with a cosolvent. However three other references that involve reactions using  $\beta$ -galactosidase use DMF (Fujimoto et al., page 157, col 1, 1<sup>st</sup> and 3<sup>rd</sup> paragraphs), DMSO (Gabelsberger et al. page 133, col 1, 1<sup>st</sup> paragraph) and dioxane (Yoshitake et al., page 396, col 2 line 1) in the formulation of their phosphate buffer. All three of these reactions use the organic solvent/phosphate buffer system successfully with  $\beta$ -galactosidase to hydrolyze a substrate. It would have been obvious to someone

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skilled in the art to use either of the three solvents in the phosphate buffer in the method of Reyes et al. Since all three share the same goal of Reyes of hydrolyzing a substrate with β-galactosidase. Each provides a reasonable expectation of success since each accomplishes the hydrolysis of their substrate using their phosphate buffer cosolvent.

The amount of the cosolvent ranges from 20% in Fujimoto et al. to 2% in Yoshitake et al. One of ordinary skill in the art would recognize that the amount of DMSO is an optimizable parameter and that the amount of solvent in the phosphate buffer would depend on the amount of enzymes in the solution along with the solubility tolerance of the substrate in the buffer as the co-solvent increases or decreases. Therefore claim 26 is rendered obvious since one of ordinary skill in the art would meet the limitation through routine optimization of the co-solvent in the reaction mixture.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

**In response to this office action the applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06).** Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

#### CONTACT INFORMATION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thane Underdahl whose telephone number is (571) 272-9042. The examiner can normally be reached during regular business hours, 8:00 to 17:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

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you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Thane Underdahl  
Art Unit 1651

Leon B. Lankford Jr  
Primary Examiner  
Art Unit 1651